

Challenge M103-3

November 2010

Nares swab: screening for Methicillin-resistant *Staphylococcus aureus*: positive

HISTORY

The sample was a simulated a nose swab obtained from a 50 year old male as a MRSA admission screen.

CMPT QA

Internal quality control testing at CMPT yielded methicillin-resistant *S. aureus*, viable for 15 days.

SURVEY RESULTS

Reference Labs: 15/15 labs reported MRSA, 15/15 labs indicated they would notify Infection Control (IC).

Identification: (Table 1) All, but one laboratory correctly reported methicillin-resistant *Staphylococcus aureus* and received a grade of 4. Laboratories that did not send a report were graded 0. Those laboratories that do not normally process this kind of sample were ungraded.

Infection control (IC) notification: (Table 2): Eighty-two laboratories mentioned they would notify IC, while 3 labs said they would notify public health (PH) and were graded 4. Three laboratories reported MRSA, but did not notify IC or PH and were graded 0.

COMMENTS ON RESULTS

Laboratories are encouraged to report “MRSA” or “presumptive MRSA” to infection control when they have sufficient information to suggest that the isolate is a *S. aureus* that is resistant to oxacillin.

This would include sufficient growth within 24

hours on an MRSA screening agar, and confirmation that the isolate is *S. aureus* (e.g. the isolate is coagulase positive by tube coagulase, latex agglutination tests or indicates positive colour on chromogenic MRSA screening medium).¹

In facilities that do not have specific infection control staff, the laboratory should notify the ward staff about the MRSA isolate and the report should include a comment code indicating isolation precautions are needed.

Recognizing that not all facilities have a designated Infection Control practitioner, CMPT will now use the phrase “Isolation Precaution Notification.”¹

One laboratory indicated that it would report the isolate to its provincial laboratory. The purpose of reporting is to ensure isolation measures are put in place for infection control. Since reporting to another laboratory would not serve this purpose, the response was graded 0.

SCREENING SITES

Anterior nares, throat, and rectum, and moist sites such as the axillae, groins and perineum have been recognized as the main sites MRSA strains colonize.

Sampling from multiple sites has shown to increase the detection of MRSA. Combined swabs from nose and throat, nose and perineum, and nose, throat and perineum identified 86%, 93% and 98% of colonized patients, respectively.²

Multiple-site screening (ideally nose, throat and perineum for most patients) is thus necessary to achieve an adequate detection rate.

Grading

Maximum grade: 8

Reporting the isolate as MRSA was graded 4.

Suggesting the isolate was vancomycin intermediate was downgraded to 3.

Laboratories that reported the isolate to IC or PH were graded 4.

Reporting to another lab, even a PH lab was graded 0. Not reporting to IC or PH was graded 0.

Table –1: Identification Results

Reported results - Identification	A	B	Total	Grade
methicillin-resistant <i>Staphylococcus aureus</i> , +/- presumptive, +/- snnp, +/- refer	68	18	87	4
<i>Staphylococcus aureus</i> , refer		1	1	4
<i>Staphylococcus aureus</i> MRSA and VISA, refer	1		1	3
snpn +/- refer	5	5	10	ungraded
no report		1	1	0
Total	74	25	99	

snpn: sample not normally processed; VISA: vancomycin intermediate *S. aureus*.

Table –2: Infection Control notification - Results

Reported results - Notification to IC	A	B	Total	Grade
yes	65	17	82	4
PH notification	1	2	3	4
snp +/- refer	5	6	11	ungraded
no report	2		2	0
Total	74	25	99	

Snp: sample not normally processed.

SCREENING METHODS

Screening for MRSA can be carried out by culture or by molecular methods.

Culture methods have become less labour intensive and more rapid by the use of chromogenic media. These media detect an enzyme characteristic of *Staphylococcus aureus* (e.g. alpha glucosidase in ChromID {bioMerieux}; phosphatase in Denim Blue medium {Oxoid}) and use cefoxitin as a selective agent, which enhances sensitivity by inducing enhanced expression of PBP 2' (2a). Different concentrations of cefoxitin are used in different chromogenic media. However, the effect on specificity due to different cefoxitin concentrations appears to be slight. These media have high specificity at 24 hours (reported to be 96-99%) and high sensitivity (70-80%). Comparisons of methods are complicated by the choice of comparator, and the gold standard used.-

The principle advantages of the chromogenic media are their low acquisition cost and low labour costs with high specificity. Their principle disadvantage remains the time taken for a positive result, although they are a major improvement over previous culture methods, for example, mannitol salt agar supplemented with cefoxitin.

Although pre-enrichment by overnight incubation in broth has been shown to augment sensitivity of culture using chromogenic media, the extended time required until results are available is a disadvantage.

Culture of MRSA screening swabs in selective broth can increase the sensitivity of the test, provided that the selective medium is not inhibitory to the MRSA strain involved. Pre-incubation in a selective enrichment broth is usually performed before real-time PCR to detect *nuc* and *mecA* genes. ⁷

Methicillin resistance determination

Oxacillin Resistance: ⁵

- *Agar dilution (MHA with 6ug/mL oxacillin and 4% NaCl):* Spot a 0.5 McFarland suspension on the agar. Incubate at 33-35 °C* for 24 hours. MRSA : >1 colony or light film of growth.

mecA-mediated oxacillin resistance:

- *Disk diffusion (30ug cefoxitin disk):* standard recommendations. Incubate at 33-35 °C* for 16-18 hours. *mecA* positive: ≤21 mm.
- *Broth microdilution (cefoxitin):* standard recommendations. Incubate at 33-35 °C* for 16-20 hours. *mecA* positive: >4 ug/mL.

*Testing at temperatures above 35°C may not detect MRSA

Automated systems, e.g., MicroScan, Vitek, and Vitek 2, and oxacillin or cefoxitin screens are commonly used to identify *S. aureus* strains as MRSA.

Rapid identification of MRSA colonies can be achieved by direct latex agglutination reaction with a monoclonal antibody directed against the variant penicillin-binding protein 2a. The method has been shown to be reliable and fast. ⁶

For chromogenic media, confirmation may not be required as indicated by the manufacturer's recommendations for use.

Molecular methods for screening

Molecular methods are based on amplification (PCR and real-time PCR) or probe-based assays for genes that are specific for MRSA. Methicillin resistance is encoded by the *mecA* gene, which is associated with a mobile element designated as staphylococcal chromosome cassette *mec* (SCC*mec*). ⁸ One of the advantages of this method is that MRSA can be identified in the sample within 24 hours. ⁷ Although the

Interesting links

MicrobeWorld - Controversies in Managing MRSA Infections: To Screen or Not to Screen? (podcast from the 2009 ICAAC)

http://www.microbeworld.org/index.php?option=com_content&view=article&id=503

ESCMID consensus on MRSA

<http://onlinelibrary.wiley.com/doi/10.1111/clm.2009.15.issue-s7/issuetoc>

processing time for these PCR tests is usually 1.5–2 hours, the total turn-around time from sampling to reporting in routine clinical practice (for example, if batching is required) may be much longer.

The sensitivity of amplification tests is high. A meta-analysis gave a mean sensitivity of 86.5%. Although they were originally intended for nasal specimens only, studies suggest a slightly augmented sensitivity when specimens from other sites were also tested.¹⁸ However, there was a slight decrease in the specificity.¹⁸

PCR systems that used unlinked primers (LightCycler and Hyplex StaphyloResist) could give false positive results in cases with dual colonization with methicillin-resistant coagulase-negative staphylococci and MSSA.⁹ The BD GenOhm, GeneXpert MRSA, and the GenoType MRSA systems overcame this problem by amplifying MRSA-specific sequences in a single locus that includes the right extremity of *SCCmec* downstream of *mecA*, and part of the adjacent *S. aureus*-specific *orfX* gene.⁴

False positives can also result from the detection of *S. aureus* strains that have lost *mecA* and become methicillin-susceptible but still retain partial *SCCmec* elements that react with the primers.¹⁰

Although specificities up to 97.4% have been found on meta-analysis of study results¹⁸, the positive predictive value would be less than 50% if the incidence of colonized patients who were tested were less than 2.6%. This low PPV has led to suggestions that positive amplification results should be confirmed with culture.

A cost effectiveness analysis by the Canadian Agency for Drugs and Technologies in Health (CADTH) found that amplification was the most cost effective strategy when all patients are isolated until found to be negative by screening. When selected patients are isolated, which is the common practice in Canadian hospitals, use of a chromogenic medium was the most cost effective strategy.¹⁷

ANTIMICROBIAL SUSCEPTIBILITY

Antimicrobial susceptibility testing need not be routinely performed or reported from this sample.

Oxacillin resistant staphylococci are resistant to

all β -lactam agents with the exception of the newer cephalosporins with anti-MRSA activity (ceftobiprole and ceftaroline, which are currently not available in Canada). According to CLSI, other β -lactam agents should be reported as resistant or should not be reported.

One laboratory indicated that this isolate showed intermediate susceptibility to vancomycin. MIC testing showed that the isolate had an MIC of 1, which is sensitive. Although not required in this case, MIC testing of MRSA clinical isolates for vancomycin can be important for therapeutic decision making.

REPORTING

It is widely accepted that rapid reporting of MRSA screening results is important for MRSA control, although the evidence base for this is limited. However, rapid reporting is of no value unless there is a rapid and appropriate response. It is essential that a plan (or care pathway) is in place, detailing who should be informed and what is to be done when an MRSA result is reported, and that these actions are implemented immediately.⁴

CLINICAL SIGNIFICANCE

MRSA is an important nosocomial pathogen in Canada. The need to have admission surveillance to screen for asymptomatic carriage of MRSA in high risk patients is recommended in Canada¹² and in some states in the United States, it is mandated by law.¹³

Community-acquired MRSA (CA-MRSA) infections have also become more prevalent in the last few years. As reported recently in the Canadian Medical Association Journal, community associated MRSA in certain populations can have increased morbidity and mortality.¹⁴ Community-acquired MRSA are usually less resistant to other antibiotics compared to hospital acquired MRSA.¹⁵ The community population, unlike patients who have been hospitalized for some time, may have been less exposed to other antibiotics.

From both the therapeutic and epidemiologic points of view, identification of carriers and patients infected with HA-MRSA and CA-MRSA is an important issue. It is critical for controlling the wide spread of multiresistant and/or highly virulent strains. The example shown by the Netherlands and Scandinavian countries –

where, after the introduction of strict monitoring of enrolled patients, the percentage of MRSA incidents was lowered and maintained at a level below 1% – shows the importance of carriage monitoring.^{7,16}

REFERENCES

1. Clinical Microbiology Proficiency Testing. M084-2:Nares (bilateral sample): Methicillin-resistant staphylococcus aureus (MRSA). notification to InfectionControl / isolation precaution notification. *CMPT Clinical Bacteriology Critiques* [serial online]. 2009. LINK: http://www.cmpt.ca/critiques_2009/m084_2_nares_mrsa_feb_09.pdf.
2. Coello R, Jimenez J, Garcia M, et al. Prospective study of infection, colonization and carriage of methicillin-resistant *Staphylococcus aureus* in an outbreak affecting 990 patients. *Eur J Clin Microbiol Infect Dis*. 1994;13:74-81.
3. Lagace-Wiens PRS, Alfa MJ, Manickam K, Harding GKM. Reductions in workload and reporting time by use of methicillin-resistant *Staphylococcus aureus* screening with MRSASelect medium compared to mannitol-salt medium supplemented with oxacillin. *J Clin Microbiol*. 2008;46:1174-1177.
4. French GL. Methods for screening for methicillin-resistant *Staphylococcus aureus* carriage. *Clin Microbiol Infect*. 2009;15 Suppl 7:10-16.
5. Clinical Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; 20th informational supplement. Wayne, PA.: Clinical and Laboratory Standards Institute; 2010:M100-S20CLSI, Wayne, PA.
6. Cavassini M, Wenger A, Jaton K, Blanc DS, Bille J. Evaluation of MRSA-screen, a simple anti-PBP 2a slide latex agglutination kit, for rapid detection of methicillin resistance in *Staphylococcus aureus*. *J Clin Microbiol*. 1999;37:1591-1594.
7. Kurlenda J, Grinholc M. Current diagnostic tools for methicillin-resistant *Staphylococcus aureus* infections. *Mol Diagn Ther*. 2010;14:73-80.
8. Katayama Y, Ito T, Hiramatsu K. A new class of genetic element, staphylococcus cassette chromosome mec, encodes methicillin resistance in *Staphylococcus aureus*. *Antimicrob Agents Chemother*. 2000;44:1549-1555.
9. Becker K, Pagnier I, Schuhen B, et al. Does nasal cocolonization by methicillin-resistant coagulase-negative staphylococci and methicillin-susceptible *Staphylococcus aureus* strains occur frequently enough to represent a risk of false-positive methicillin-resistant *S. aureus* determinations by molecular methods? *J Clin Microbiol*. 2006;44:229-231.
10. Malhotra-Kumar S, Haccuria K, Michiels M, et al. Current trends in rapid diagnostics for methicillin-resistant *Staphylococcus aureus* and glycopeptide-resistant enterococcus species. *J Clin Microbiol*. 2008;46:1577-1587.
11. Ritchie K, Bradbury I, Craig J et al. The clinical and cost effectiveness of screening for methicillin-resistant *Staphylococcus aureus* (MRSA). NHS Quality Improvement Scotland: Health Technology Assessment Report 9, 2007. LINK: http://www.nhshealthquality.org/nhsqis/files/PatientSafety_HTA9_MRSA_advice_Oct07.pdf
12. Guidelines for the prevention and management of community-associated methicillin-resistant *Staphylococcus aureus*: A perspective for Canadian health care practitioners. *Can J Infect Dis Med Microbiol*. 2006;17:4C-24C. LINK: <http://www.pulsus.com/journals/JnlSupToc.jsp?CurrPg=journal&jnlKy=3&supKy=380>
13. Weber SG, Huang SS, Oriola S, et al. Legislative mandates for use of active surveillance cultures to screen for methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci: Position statement from the joint SHEA and APIC task force. *Am J Infect Control*. 2007;35:73-85.
14. Gilbert M, MacDonald J, Gregson D, et al. Outbreak in Alberta of community-acquired (USA300) methicillin-resistant *Staphylococcus aureus* in people with a history of drug use, homelessness or incarceration. *CMAJ*. 2006;175:149-154.
15. Hussain FM, Boyle-Vavra S, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic. *Pediatr Infect Dis J*. 2001;20:763-767.
16. Vos MC, Behrendt MD, Melles DC, et al. 5 years of experience implementing a methicillin-resistant *Staphylococcus aureus* search and destroy policy at the largest university medical center in the Netherlands. *Infect Control Hosp Epidemiol*. 2009;30:977-984.